

WHAT IS CLAIMED IS:

1. A method for sterilizing a preparation of one or more glycosidases that is sensitive to radiation, said method comprising irradiating said preparation of one or more glycosidases with radiation for a time effective to sterilize said preparation of one or more glycosidases at a rate effective to sterilize said preparation of one or more glycosidases and to protect said preparation of one or more glycosidases from said radiation.

but a 2. A method for sterilizing a preparation of one or more glycosidases that is sensitive to radiation, said method comprising:

(i) adding to said preparation of one or more glycosidases at least one stabilizer in an amount effective to protect said preparation of one or more glycosidases from said radiation; and
(ii) irradiating said preparation of one or more glycosidases with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more glycosidases.

3. A method for sterilizing a preparation of one or more glycosidases that is sensitive to radiation, said method comprising:

(i) reducing the residual solvent content of said preparation of one or more glycosidases to a level effective to protect said preparation of one or more glycosidases from said radiation; and
(ii) irradiating said preparation of one or more glycosidases with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more glycosidases.

4. A method for sterilizing a preparation of one or more glycosidases that is sensitive to radiation, said method comprising:

(i) reducing the temperature of said preparation of one or more glycosidases to a level effective to protect said preparation of one or more glycosidases from said radiation; and
(ii) irradiating said preparation of one or more glycosidases with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more glycosidases.

5. A method for sterilizing a preparation of one or more glycosidases that is sensitive to radiation, said method comprising:

(i) applying to said preparation of one or more glycosidases at least one stabilizing process selected from the group consisting of

(a) reducing the residual solvent content of said preparation of one or more glycosidases,

(b) reducing the temperature of said preparation of one or more glycosidases, and

(c) adding at least one stabilizer to said preparation of one or more glycosidases; and

(ii) irradiating said preparation of one or more glycosidases with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more glycosidases, wherein said at least one stabilizing process and the rate of irradiation are together effective to protect said preparation of one or more glycosidases from said radiation.

6. A method for sterilizing a preparation of one or more glycosidases that is sensitive to radiation, said method comprising:

(i) applying to said preparation of one or more glycosidases at least two stabilizing processes selected from the group consisting of :

(a) reducing the residual solvent content of said preparation of one or more glycosidases,

(b) reducing the temperature of said preparation of one or more glycosidases, and

(c) adding at least one stabilizer to said preparation of one or more glycosidases; and

(ii) irradiating said preparation of one or more glycosidases with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more glycosidases, wherein said at least two stabilizing processes are together effective to protect said preparation of one or more glycosidases from said radiation and further wherein said at least two stabilizing processes may be performed in any order.

7. The method according to claim 3, 5 or 6, wherein said solvent is water.

8. The method according to claim 7, wherein said residual water content is reduced by the addition of an organic solvent.

9. The method according to claim 3, 5 or 6, wherein said solvent is an organic solvent.

10. The method according to claim 3, 5 or 6, wherein said preparation of one or more glycosidases is suspended in an organic solvent following reduction of said residual solvent content.

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11. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is not more than about 3.0 kGy/hour.

12. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is not more than about 2.0 kGy/hr.

13. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is not more than about 1.0 kGy/hr.

14. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is not more than about 0.3 kGy/hr.

15. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is more than about 3.0 kGy/hour.

16. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is at least about 6.0 kGy/hour.

17. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is at least about 18.0 kGy/hour.

18. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is at least about 30.0 kGy/hour.

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19. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is at least about 45 kGy/hour.

20. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said preparation of one or more glycosidases is maintained in a low oxygen atmosphere.

21. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said preparation of one or more glycosidases is maintained in an atmosphere comprising at least one noble gas.

22. The method according to claim 21, wherein said noble gas is argon.

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23. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said preparation of one or more glycosidases is maintained in a vacuum.

24. The method according to claim 3, 5 or 6, wherein said residual solvent content is reduced by a method selected from the group consisting of lyophilization, drying, concentration, addition of solute, evaporation, chemical extraction, spray-drying and vitrification.

25. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 15%.

26. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 10%.

27. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 3%.

28. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 2%.

29. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 1%.

30. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 0.5%.

31. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 0.08%.

Sub a4) 32. The method according to claim 1, 2, 3, 4, 5 or 6, wherein at least one sensitizer is added to said preparation of one or more glycosidases prior to said step of irradiating said preparation of one or more glycosidases.

33. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said preparation of one or more glycosidases contains at least one biological contaminant or pathogen selected from the group consisting of viruses, bacteria, yeasts, molds, fungi, parasites, and prions or similar agents responsible, alone or in combination, for TSEs.

34. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is an antioxidant.

35. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is a free radical scavenger.

36. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is a combination stabilizer.

37. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is a ligand.

38. The method according to claim 37, wherein said ligand is heparin.

39. The method according to claim 37, wherein said ligand is a substrate or substrate analog of at least one glycosidase contained in said preparation of one or more glycosidases.

40. The method according to claim 2, 5 or 6, wherein said at least one stabilizer reduces damage due to reactive oxygen species.

41. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is selected from the group consisting of: ascorbic acid or a salt or ester thereof; glutathione; 6-hydroxy-2,5,7,8-tetramethylchouroman-2-carboxylic acid; uric acid or a salt or ester thereof; methionine; histidine; N-acetyl cysteine; lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; propyl gallate and mixtures of two or more thereof.

42. The method according to claim 41, wherein said mixtures of two or more additional stabilizers are selected from the group consisting of: mixtures of ascorbic acid, or a salt or ester thereof, and uric acid, or a salt or ester thereof; mixtures of ascorbic acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchouroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchouroman-2-carboxylic acid; and mixtures of uric acid, or a salt or ester thereof; lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; propyl gallate and 6-hydroxy-2,5,7,8-tetramethylchouroman-2-carboxylic acid.

43. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is a dipeptide stabilizer.

44. The method according to claim 43, wherein said dipeptide stabilizer is selected from the group consisting of glycyl-glycine (Gly-Gly), carnosine and anserine.

Sur A5 45. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is corpuscular radiation or electromagnetic radiation, or a mixture thereof.

46. The method according to claim 45, wherein said electromagnetic radiation is selected from the group consisting of radio waves, microwaves, visible and invisible light, ultraviolet light, x-ray radiation, gamma radiation and combinations thereof.

Subseq 47. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is gamma radiation.

48. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is E-beam radiation.

49. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is visible light.

50. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is ultraviolet light.

51. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is x-ray radiation.

52. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is polychromatic visible light.

53. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is infrared.

54. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is a combination of one or more wavelengths of visible and ultraviolet light.

55. The method according to claim 1, 2, 3, 5 or 6, wherein said irradiation is conducted at ambient temperature.

56. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said irradiation is conducted at a temperature below ambient temperature.

57. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said irradiation is conducted below the freezing point of said preparation of one or more glycosidases.

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58. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said irradiation is conducted below the eutectic point of said preparation of one or more glycosidases.

59. The method according to claim 1, 2, 3, 5 or 6, wherein said irradiation is conducted at a temperature above ambient temperature.

60. A composition comprising at least one preparation of one or more glycosidases and at least one stabilizer in an amount effective to preserve said preparation of one or more glycosidases for its intended use following sterilization with radiation.

61. A composition comprising at least one preparation of one or more glycosidases, wherein the residual solvent content of said preparation of one or more glycosidases is at a level effective to preserve said preparation of one or more glycosidases for its intended use following sterilization with radiation.

62. The composition of claim 61, wherein said residual solvent content is less than about 15%.

63. The composition of claim 61, wherein said residual solvent content is less than about 10%.

64. The composition of claim 61, wherein said residual solvent content is less than about 5%.

65. The composition of claim 61, wherein said residual solvent content is less than about 2%.

66. The composition of claim 61, wherein said residual solvent content is less than about 1%.

67. The composition of claim 61, wherein said residual solvent content is less than about 0.5%.

68. The composition of claim 61, wherein said residual solvent content is less than about 0.08%.

69. The composition of claim 60 or 61, wherein said preparation of one or more glycosidases is glassy or vitrified.

70. The composition of claim 60 or 61, wherein said preparation of one or more glycosidases contains at least one galactosidase.

71. The composition of claim 61, wherein the total protein concentration of said preparation of one or more glycosidases is at least about 0.5%.

72. The composition of claim 61, wherein the total protein concentration of said preparation of one or more glycosidases is at least about 1%.

73. The composition of claim 61, wherein the total protein concentration of said preparation of one or more glycosidases is at least about 5%.

74. The composition of claim 61, wherein the total protein concentration of said preparation of one or more glycosidases is at least about 10%.

75. The composition of claim 61, wherein the total protein concentration of said preparation of one or more glycosidases is at least about 15%.

76. The composition of claim 61, wherein the total protein concentration of said preparation of one or more glycosidases is at least about 20%.

77. The composition of claim 61, wherein the total protein concentration of said preparation of one or more glycosidases is at least about 25%.

78. The composition of claim 61, wherein the total protein concentration of said preparation of one or more glycosidases is at least about 50%.

79. A method of treating a glycosidase deficiency in a mammal comprising administering to a mammal in need thereof an effective amount of a preparation of one or more glycosidases which has been sterilized according to the method according to claim 1, 2, 3, 4, 5 or 6.

80. The method according to claim 79, wherein said mammal is a human.

81. The method according to claim 79, wherein said glycosidase deficiency is Fabry disease.

82. The method according to claim 79, wherein said preparation of one or more glycosidases comprises α -galactosidase.

83. A method of improving digestion in a mammal comprising administering to a mammal in need thereof an effective amount of a preparation of one or more glycosidases which has been sterilized according to the method according to claim 1, 2, 3, 4, 5 or 6.

84. The method according to claim 80, wherein said mammal is a human.

85. The method according to claim 80, wherein said preparation of one or more glycosidases comprises at least one galactosidase.